

Mechanism of action and research progress of Banxia Xiexin Tang in the treatment of gastric cancer

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Abstract: Half-summer diarrhea heart soup is a classic formula in the Treatise on Typhoid Miscellaneous Diseases. It has been used for treating a variety of spleen and stomach disorders based on the symptoms of plumpness under the heart and the mixture of cold and heat. Recent studies have found that this formula has multi-target effects in regulating gastrointestinal function, anti-inflammatory, anti-tumor and metabolic diseases. In this paper, we will systematically describe its chemical composition, pharmacological mechanism and clinical research progress in the treatment of gastric cancer, so as to provide more scientific and accurate data support for future clinical application. With the development of modern society and the improvement of economic level, people's living habits have undergone significant changes, and the occurrence of diseases has followed. gastric cancer (GC) is one of the tumors with high prevalence in the world, and the survival rate of patients within 5 years is only about 20%^[1]. The number of incidence and death of gastric cancer in China is the highest in the world, accounting for about 43.9% and 48.6%^[2]. The emergence of new treatment modalities such as immunization and targeted therapy has improved the prognosis of patients to some extent. In Chinese medicine, cancer is referred to as the accumulation of obstruction in the abdomen, which has been recorded by the ancients. With the development of modern science and technology, the mechanism of action of Banxia Xiexin Tang in treating gastric cancer has been gradually clarified, and this paper aims to summarize the mechanism of action and research progress of hemixia laxative heart soup.

1. Overview of Banxia Xiexin Tang

1.1 Traceability of Banxia Xiexin Decoction

Banxia Xiexin Tang (BXT) is a classic formula originated from The Treatise on Typhoid Miscellaneous Diseases, which has been deeply studied by medical practitioners through the ages. The Treatise on Typhoid Fever says: "But fullness without pain, this is a plague, Chai Hu is

not in the middle with it, it is appropriate to Banxia Xiexin Decoction". The "Essentials of the Golden Chamber" recorded: "If there is vomiting accompanied by borborygmus and a feeling of fullness and oppression below the heart, Banxia Xiexin Decoction should be used for treatment". According to the original record, it is composed of seven herbs, namely *Pinellia ternata* (half a sheng, washed), *Scutellaria baicalensis*, dried ginger, *Coptis chinensis*, ginseng, roasted licorice root, and twelve Chinese dates. In the formula, *Scutellaria baicalensis* and *Coptis chinensis* are bitter and cold in nature, clearing heat and drying dampness. Their pungency and bitterness act on the stomach, assisting the spleen in its pivotal movement and transportation function. *Pinellia ternata* and dried ginger are pungent and hot. Their pungency and sweetness act on the spleen, relieving chest stuffiness, resolving masses, suppressing nausea and vomiting, and helping the stomach receive and digest food. *Codonopsis pilosula*, roasted licorice root, and Chinese dates work together to tonify the body, replenish qi and yuan, assist the spleen in receiving and transporting, and promote the ascent of the clear and the descent of the turbid^[3]. This formula was formulated due to improper purgation in Shaoyang disease and evolved from the Minor Bupleurum Decoction for Shaoyang syndrome. It is a classic famous formula that combines pungent-opening and bitter-dropping methods to relieve the "fullness" in the semi-exterior and semi-interior regions. It mainly treats the syndrome of fullness with concurrent deficiency and excess, as well as intermingled cold and heat. Banxia Xiexin Tang (BXT) treats the syndrome of fullness with intermingled cold and heat. Through the summarization and development by successive generations of physicians, it has been found that it can treat various digestive tract diseases with the syndrome of intermingled cold and heat, such as gastric ulcer, reflux esophagitis, cholecystitis, etc. With the development of modern research methods, the multi-target and multi-pathway action characteristics of this formula have been gradually revealed, making it a typical case in the modern research of traditional Chinese medicine.

1.2 Modern pharmacological study of BXT

In recent years, a large number of experimental studies and clinical applications have found that BXT has good clinical performance in the treatment of gastric cancer, regulation of blood glucose, regulation of intestinal flora, regulation of neurotransmitters, etc. In this formula, β -hydroxybenzoic acid (β -hydroxybenzoic acid) is found in the formula. In the formula, there are β -sitosterol, stigmasterol and other substances in hemixia; berberine, palmatine, and flavonoids in Huanglian; ginseng saponin Rg3 and ginseng polysaccharides in ginseng; and triterpenoids, glycosides, amino acids and flavonoids in jujubes, etc.[4] ; and licorice contains glycyrrhetic acid, glycyrrhizin, etc.[5] . *Scutellaria baicalensis*, the main chemical components include flavonoids, volatile oils, terpenoids, organic acids, etc.[6] Dried ginger, which contains volatile oil, curcumin-like compounds, diphenylheptane-like compounds, amino acids, etc.[7] . Experimental studies have shown that BXT inhibits excessive apoptosis of gastric mucosal epithelial cells, enhances the expression of Bcl-2 mRNA, inhibits the activation of cystatin-3 (Caspase-3) zymogen, and thus protects the mucosa of the gastrointestinal tract[8] .

1.3 Clinical Application of Banxia Xiexin Tang

Semixia Laxative Heart Soup is effective in the treatment of digestive disorders, such as chronic gastritis, *Helicobacter pylori* infection, ulcerative colitis, gastric ulcer, gastroesophageal reflux disease and irritable bowel syndrome. Li Yanying divided 50 patients with chronic gastritis into 2 groups, the control group was treated with a standard western medicine treatment program, and the treatment group was treated with Banxia Xiexin Tang and acupuncture therapy, and the results showed that Banxia Xiexin Tang could improve inflammatory factors, alleviate the clinical

symptoms of the patients, and contribute to the rapid recovery. Zhao Yingying et al.^[9] found that half-xia laxative heart soup combined with tetrapuncture for gastric ulcer treatment, and the results showed that the combination of traditional Chinese and Western medicine therapy can rapidly reduce patients' symptoms such as early satiety, epigastric pain, nausea, postprandial bloating, ergotism, etc., and it can remove *H. pylori* bacteria, regulate the inflammatory factors, and promote the rapid recovery of gastric function. Li Muroji et al.^[10] showed that Banxia Xiexin Tang improved the degree of colonic damage and protected and repaired the intestinal mucosa through the expression of TLRs/NF- κ B/MyD88 signaling pathway and its related factors. Half-xia laxative heart soup also has good efficacy in the treatment of dementia, insomnia, post-circulatory ischemic vertigo, and other neurological disorders. Feng Yingying^[11] The treatment of 46 patients with posterior circulation ischemic vertigo with the addition of Banxia Xiexin Tang has an overall effective rate of 95.65%, which is better than that of the control group (82.50%), and reduces the occurrence of adverse reactions. Zheng Mingcui^[12] study showed that by attenuating NLRP3 inflammatory vesicle interactions, Banxia Xiexin Tang helps to alleviate neuroinflammation and exerts a protective effect on the nervous system, thus preventing the development of dementia. Experimental studies^[13] have shown that by elevating the levels of dopamine and 5-hydroxytryptamine in the brain regions, half-haxia laxative heart soup enhances the expression of brain-derived neurofactors in the frontal cortex, which in turn improves the release of neurotransmitters, and ultimately improves the learning ability of senescent rats. With the continuous deepening of clinical and experimental, more experiments have proved that Banxia Xiexin Tang also has good effect in the treatment of endocrine diseases, respiratory diseases, dermatology, gynecology and so on.

2. Research Progress of Banxia Xiexin Tang in Treating Gastric Cancer

2.1 Progress of clinical research on the treatment of gastric cancer

with Banxia Xiexin Tang Chemotherapy is the main means of treating gastric cancer at present, but the side effects on the digestive tract often tend to affect the completion rate and efficacy of chemotherapy and lead to the progression of the disease, especially the symptoms of gastric distension and fullness, nausea and vomiting, anorexia, diarrhea and abdominal pain, etc., which have affected the quality of life of patients.^[14] , therefore, many medical practitioners in clinics have alleviated the side effects on the digestive tract by using Banxia Xiexin Tang to alleviate the symptoms of chemotherapy. Therefore, in clinical practice, many medical practitioners use Banxia Xiexin Tang to reduce the side effects of chemotherapy on the digestive tract. According to Li training, "Nourishing the positive accumulation will eliminate itself", to cultivate positive qi, the first step is to nourish the spleen and stomach, and the Banxia Xiexin Tang can adjust the function of the spleen and stomach, so as to achieve the purpose of nourishing the positive^[15] . Zhang Ruoyan^[16] believes that in clinical practice, it has better efficacy for diarrhea caused by chemotherapy and prevention of delayed-onset diarrhea. In addition, Banxia Xiexin Tang can promote the recovery of postoperative gastric cancer patients. Postoperative gastric cancer can cause many complications, which seriously affects the postoperative life of patients, especially bile reflux gastritis, which is mainly manifested as abdominal distension, acid reflux, heartburn, vomiting, and even bleeding, etc. Wang Hongyan et al.^[17] found that the addition of Banxia Xiexin Tang could be effective in preventing and controlling bile reflux gastritis after gastric cancer operation. Some scholars have also found that Banxia Xiexin Tang can also treat precancerous gastric lesions. Xu Sheng et al.^[18] found that the addition and subtraction of Banxia Xiexin Tang can improve the clinical symptoms of patients with precancerous lesions of chronic atrophic gastritis, such as the reduction of intestinal epithelial metaplasia, glandular atrophy, and heterotopic

hyperplasia, with a higher cure rate than that of gastric Fuchun. Chen Youming[19] believes that Banxia Xiexin Tang can not only effectively treat chronic atrophic gastritis, but also has significant efficacy on peptic ulcer infected with *Helicobacter pylori*, with strong bacteriostatic effect.

2.2 Progress of experimental research on the treatment of gastric cancer with Banxia Xiexin Tang

Currently, experimental research has found that Banxia Xiexin Tang can reduce the mechanism of toxic side effects of chemotherapy, promote apoptosis of gastric cancer cells, and inhibit peritoneal metastasis of gastric cancer cells. Shi Jiawen et al.[20] found that Banxia Xiexin Tang can effectively improve intestinal mucosal damage, improve the body mass of mice, and prevent delayed diarrhea in irinotecan-induced mice, and its mechanism of action is related to the increase of serum IL-15 level and the decrease of β -glucuronidase activity of small intestinal contents. Studies have shown that[21] Banxia Xiexin Tang can adjust the local gastrointestinal tissues, central and blood growth inhibitin content, which is manifested as it can antagonize atropine-induced slowing down of gastric emptying and small intestinal propulsion, and also inhibit small intestinal propulsion hyperactivity induced by neostigmine, which is related to the adjustment of the local gastrointestinal tissues, central and blood growth inhibitin content. The promotion of apoptosis of gastric cancer cells by Banxia Xiexin Tang is a key link in the treatment of gastric cancer, Gao Xiaoling et al.[22] found that Banxia Xiexin Tang can inhibit gastric cancer SGC-7901 cells, increase the proportion of cells in the G1 phase, and promote apoptosis of gastric cancer cells. Wang Jing et al.[23] found in their experiments that half-summer diarrhea heart soup containing serum could protect the damage of peritoneal mesothelial cells after the induction of gastric cancer microenvironment. Gastric cancer cells are prone to dissemination and implantation in the peritoneal cavity, so it is exceptionally important to prevent the dissemination and implantation of gastric cancer cells, and numerous scholars have found the efficacy of Hanxia laxative heart soup in inhibiting the dissemination and implantation of gastric cancer cells. Li Dongfeng et al.[24] found that the serum of Bianxia Laxingxin Tang could inhibit the proliferation and invasive metastasis of the peritoneal high-metastatic-potential cell line GC9811-P of human gastric cancer in their experiments. Yang Berlin et al.[25] showed that the effect of half-xia laxative heart soup and different combinations of drug-containing serums in inhibiting the abnormal proliferation of bone marrow mesenchymal stem cells (BMSCs) in the microenvironment of gastric cancer was significant, and the effect of the whole formula of half-xia laxative heart soup was the most effective. In addition, other studies have shown that BMSCs can treat precancerous lesions and prevent gastric cancer.

3. Conclusion

Banxia Xiexin Tang is from Zhang Zhongjing's "Treatise on Typhoid Fever", which is used for the treatment of cardiac plaque under the heart of cold and heat, and it is a representative formula for the treatment of middle-heat diseases. It is a representative formula for treating middle Jiao disease, which has been recorded by many medical doctors throughout the ages. Stomach cancer has a high degree of malignancy and poor prognosis, and the treatment of stomach cancer by western medicine has limitations at present, so most scholars and patients hope to treat it by means of combining traditional Chinese and western medicines. With the development of science and technology, the mechanism of Banxia Xiexin Tang in treating gastric cancer has been clarified gradually, and it has been widely applied in clinical practice. However, at present, there are fewer experimental data, smaller sample sizes in clinical studies, lack of large-sample, multicenter, randomized, controlled, double-blind clinical evidence, unclear molecular mechanisms, and lack of

in-depth studies. In the future, more in-depth research can be carried out in these aspects to provide more scientific data support for clinical applications.

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